## CARDIZEM

(Diltiazem)



## Description

Amlodipine, bepridil, diltiazem, felodipine, flunarizine, isradipine, nicardipine, nifedipine, nimodipine, and verapamil belong to the group of medicines called calcium channel blocking agents.

Calcium channel blocking agents affect the movement of calcium into the cells of the heart and blood vessels. As a result, they relax blood vessels and increase the supply of blood and oxygen to the heart while reducing its workload.

Some of the calcium channel blocking agents are used to relieve and control angina pectoris (chest pain). Some are also used to treat high blood pressure (hypertension). High blood pressure adds to the workload of the heart and arteries. If it continues for a long time, the heart and arteries may not function properly. This can damage the blood vessels of the brain, heart, and kidneys, resulting in a stroke, heart failure, or kidney failure. High blood pressure may also increase the risk of heart attacks. These problems may be less likely to occur if blood pressure is controlled.

Flunarizine is used to prevent migraine headaches.

Nimodipine is used to prevent and treat problems caused by a burst blood vessel around the brain (also known as a ruptured aneurysm or subarachnoid hemorrhage).

Other calcium channel blocking agents may also be used for these and other conditions as determined by your doctor.

These medicines are available only with your doctor's prescription, in the following dosage forms:

#### Parenteral

- Diltiazem
- o Injection (U.S. and Canada)
- Verapamil
- o Injection (U.S. and Canada)

### **Before Using This Medicine**

In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For the calcium channel blocking agents, the following should be considered:

**Allergies**—Tell your doctor if you have ever had any unusual or allergic reaction to amlodipine, bepridil, diltiazem, felodipine, flunarizine, isradipine, nicardipine, nifedipine, nimodipine, or verapamil. Also tell your health care professional if you are allergic to any other substances, such as foods, preservatives, or dyes.

**Pregnancy**—Calcium channel blocking agents have not been studied in pregnant women. However, studies in animals have shown that large doses of calcium channel blocking agents cause birth defects, prolonged pregnancy, poor bone development in the offspring, and stillbirth.

**Breast-feeding**—Although bepridil, diltiazem, nifedipine, verapamil, and possibly other calcium channel blocking agents, pass into breast milk, they have not been reported to cause problems in nursing babies.

**Children**—Although there is no specific information comparing use of this medicine in children with use in other age groups, it is not expected to cause different side effects or problems in children than it does in adults.

**Older adults**—Elderly people may be especially sensitive to the effects of calcium channel blocking agents. This may increase the chance of side effects during treatment. A lower starting dose may be required.

**Other medicines**—Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases, your doctor may want to change the dose, or other precautions may be necessary. When taking calcium channel blocking agents it is especially important that your health care professional know if you are taking any of the following:

- Acetazolamide (e.g., Diamox) or
- Amphotericin B by injection (e.g., Fungizone) or
- Corticosteroids (cortisone-like medicine) or
- Dichlorphenamide (e.g., Daranide) or

## CARDIZEM

(Diltiazem)

- Diuretics (water pills) or
- Methazolamide (e.g., Naptazane)—These medicines can cause hypokalemia (low levels of potassium in the body), which can increase the unwanted effects of bepridil
- Beta-adrenergic blocking agents (acebutolol [e.g., Sectral], atenolol [e.g., Tenormin], betaxolol [e.g., Kerlone], carteolol [e.g., Cartrol], labetalol [e.g., Normodyne], metoprolol [e.g., Lopressor], nadolol [e.g., Corgard], oxprenolol [e.g., Trasicor], penbutolol [e.g., Levatol], pindolol [e.g., Visken], propranolol [e.g., Inderal], sotalol [e.g., Sotacor], timolol [e.g., Blocadren])—Effects of both may be increased. In addition, unwanted effects may occur if a calcium channel blocking agent or a beta-blocking agent is stopped suddenly after both have been used together
- Carbamazepine (e.g., Tegretol) or
- Cyclosporine (e.g., Sandimmune) or
- Procainamide (e.g., Pronestyl) or
- Quinidine (e.g., Quinidex)—Effects of these medicines may be increased if they are used with some calcium channel blocking agents
- Digitalis glycosides (heart medicine)—Effects of these medicines may be increased if they are used with some calcium channel blocking agents
- Disopyramide (e.g., Norpace)—Effects of some calcium channel blocking agents on the heart may be increased
- Erythromycin (e.g., Ery-Tab)—Should not be used together with calcium channel blocking agents, especially diltiazem or verapamil; severe heart problems may result.
- Grapefruit juice—Effects of felodipine may be increased. No effects on amlodipine.

Also, tell your health care professional if you are using any of the following medicines in the eye:

- Betaxolol (e.g., Betoptic) or
- · Levobunolol (e.g., Betagan) or
- Metipranolol (e.g., OptiPranolol) or
- Timolol (e.g., Timoptic)—Effects on the heart and blood pressure may be increased **Other medical problems**—The presence of other medical problems may affect the use of the calcium channel blocking agents. Make sure you tell your doctor if you have any other medical problems, especially:
- Congestive heart failure—Calcium channel blocking agents may make this condition worse. Do not take diltiazem if you have a history of heart attacks.
- Heart rhythm problems (history of)—Bepridil can cause serious heart rhythm problems
- Kidney disease or
- Liver disease—Effects of the calcium channel blocking agent may be increased
- Mental depression (history of)—Flunarizine may cause mental depression
- Parkinson's disease or similar problems—Flunarizine can cause parkinsonian-like effects
- Other heart or blood vessel disorders—Calcium channel blocking agents may make some heart conditions worse

### **Proper Use of This Medicine**

Take this medicine exactly as directed even if you feel well and do not notice any signs of chest pain. Do not take more of this medicine and do not take it more often than your doctor ordered. Do not miss any doses. For patients taking *amlodipine*:

• Your doctor may suggest that you change your diet and eat foods that are low in salt and fat. Losing weight will help your blood pressure along with your medicine. Talk to your doctor about the best diet for you.

For patients taking bepridil:

• If this medicine causes upset stomach, it can be taken with meals or at bedtime.

For patients taking diltiazem extended-release capsules or tablets:

- Swallow the capsule or tablet whole, without crushing or chewing it.
- Do not change to another brand without checking with your physician. Different brands have different doses. If you refill your medicine and it looks different, check with your pharmacist.

## CARDIZEM

(Diltiazem)

- You should take *Cardizem LA* at about the same time once each day either in the morning or at bedtime. If you have questions about when to take your medicine, ask your doctor. For patients taking *felodipine*:
- Do not take this medicine with grapefruit juice.

For patients taking verapamil extended-release capsules:

- Swallow the capsule whole, without crushing or chewing it.
- If you have trouble swallowing capsules, you may open the verapamil capsule and mix the medicine with applesauce. Mix only one dose at a time just before taking it. *Do not mix any doses to save for later*, because the medicine may change over time and may not work properly.

For patients taking felodipine or nifedipine extended-release tablets:

- Swallow the tablet whole, without breaking, crushing, or chewing it.
- If you are taking *Adalat XL* or *Procardia XL*, you may sometimes notice what looks like a tablet in your stool. That is just the empty shell that is left after the medicine has been absorbed into your body.
- If you are taking *Adalat CC*, take the medicine on an empty stomach

For patients taking verapamil extended-release tablets:

- Swallow the tablet whole, without crushing or chewing it. However, if your doctor tells you to, you may break the tablet in half.
- Take the medicine with food or milk.

For patients taking this medicine for high blood pressure:

- In addition to the use of the medicine your doctor has prescribed, appropriate treatment for your high blood pressure may include weight control and care in the types of food you eat, especially foods high in sodium (salt). Your doctor will tell you which factors are most important for you. You should check with your doctor before changing your diet.
- Many patients who have high blood pressure will not notice any signs of the problem. In fact, many may feel normal. It is very important that you *take your medicine exactly as directed* and that you keep your appointments with your doctor even if you feel well.
- Remember that this medicine will not cure your high blood pressure but it does help control it. Therefore, you must continue to take it as directed if you expect to lower your blood pressure and keep it down. You may have to take high blood pressure medicine for the rest of your life. If high blood pressure is not treated, it can cause serious problems such as heart failure, blood vessel disease, stroke, or kidney disease.

# Dosing-

The dose of these medicines will be different for different patients. *Follow your doctor's orders or the directions on the label.* The following information includes only the average doses of these medicines. *If your dose is different, do not change it* unless your doctor tells you to do so.

The number of capsules or tablets that you take depends on the strength of the medicine. Also, the number of doses you take each day, the time allowed between doses, and the length of time you take the medicine depend on the medical problem for which you are taking calcium channel blocking agents. For amlodipine

- For oral dosage form (tablets):
- o For angina (chest pain):
- Adults—5 to 10 milligrams (mg) once a day.
- Children 6 years of age and older—2.5 to 5 mg once a day.
- Children younger than 6 years of age—Use must be determined by your doctor.

Note: Elderly patients or patients determined by your health care professional may be started on a lower dose.

- For high blood pressure:
- Adults—5 to 10 mg once a day.
- Children—Use must be determined by your doctor.

Note: Elderly patients or patients determined by your health care professional may be started on 2.5 mg once a day.

### For bepridil

• For oral dosage form (tablets):

## CARDIZEM

(Diltiazem)

- o For angina (chest pain):
- Adults—200 to 300 milligrams (mg) once a day.
- Children—Use and dose must be determined by your doctor.

#### For diltiazem

- For long-acting oral dosage form (extended-release capsules and tablets):
- o For angina (chest pain):
- Adults and teenagers:
- For Cardizem LA: 180 mg once a day in the morning or at bedtime.
- Children—Dose must be determined by your doctor.
- o For high blood pressure:
- Adults and teenagers:
- For Cardizem CD or Cardizem LA or Dilacor-XR: 180 to 240 milligrams (mg) once a day.
- For Cardizem SR: 60 to 120 mg two times a day.
- Children—Dose must be determined by your doctor.
- For regular (short-acting) oral dosage form (tablets):
- For angina (chest pain):
- Adults and teenagers—30 mg three or four times a day. Your doctor may gradually increase your dose as needed.
- Children—Dose must be determined by your doctor.
- For *injection* dosage form:
- o For arrhythmias (irregular heartbeat):
- Adults and teenagers—Dose is based on body weight and must be determined by your doctor.
- Children—Use and dose must be determined by your doctor.

#### For felodipine

- For *long-acting oral* dosage form (extended-release tablets):
- o For high blood pressure:
- Adults—5 to 10 milligrams (mg) once a day.
- Children—Use and dose must be determined by your doctor.
- o For angina (chest pain):
- Adults—10 mg once a day.
- Children—Use and dose must be determined by your doctor.

#### For flunarizine

- For oral dosage form (capsules):
- o To prevent headaches:
- Adults—10 milligrams (mg) once a day in the evening.
- Children—Dose must be determined by your doctor.

# For isradipine

- For oral dosage form (capsules):
- o For high blood pressure:
- Adults—2.5 milligrams (mg) two times a day. Your doctor may increase your dose as needed.
- Children—Use and dose must be determined by your doctor.

# For nicardipine

- For oral dosage form (capsules):
- o For high blood pressure or angina (chest pain):
- Adults and teenagers—20 milligrams (mg) three times a day.
- Children—Dose must be determined by your doctor.

### For nifedipine

- For regular (short-acting) oral dosage form (capsules):
- o For high blood pressure or angina (chest pain):
- Adults and teenagers—10 milligrams (mg) three times a day. Your doctor may increase your dose as needed.
- Children—Dose must be determined by your doctor.
- For *long-acting oral* dosage form (extended-release tablets):
- o For high blood pressure or angina (chest pain):
- Adults and teenagers:

## **CARDIZEM**

(Diltiazem)

- For Adalat CC, Adalat XL or Procardia XL: 30 or 60 mg once a day. Your doctor may increase your dose as needed.
- For Adalat PA: 10 or 20 mg two times a day. Your doctor may increase your dose as needed.
- Children—Dose must be determined by your doctor.

#### For nimodipine

- For *oral* dosage form (capsules):
- To treat a burst blood vessel around the brain:
- Adults—60 milligrams (mg) every four hours.
- Children—Dose must be determined by your doctor.

### For verapamil

- For regular (short-acting) oral dosage form (tablets):
- For angina (chest pain), arrhythmias (irregular heartbeat), or high blood pressure:
- Adults and teenagers—40 to 120 milligrams (mg) three times a day. Your doctor may increase your dose as needed.
- Children—Dose is based on body weight and must be determined by your doctor. The usual dose
  is 4 to 8 mg per kilogram (kg) (1.82 to 3.64 mg per pound) of body weight a day. This is divided into
  smaller doses.
- For long-acting oral dosage form (extended-release capsules):
- o For high blood pressure:
- Adults and teenagers
- For Verelan: 240 to 480 mg once a day
- For Verelan PM: 200 mg once a day at bedtime
- Children—Dose must be determined by your doctor.
- For long-acting oral dosage form (extended-release tablets):
- o For high blood pressure:
- Adults and teenagers—120 mg once a day to 240 mg every twelve hours.
- Children—Dose must be determined by your doctor.
- For injection dosage form:
- o For arrhythmias (irregular heartbeat):
- Adults—5 to 10 mg slowly injected into a vein. The dose may be repeated after thirty minutes.
- Children—Dose is based on body weight and must be determined by your doctor.
- Infants up to 1 year of age: 100 to 200 micrograms (mcg) per kg (45.5 to 90.9 mcg per pound) of body weight injected slowly into a vein. The dose may be repeated after thirty minutes.
- Children 1 to 15 years of age: 100 to 300 mcg per kg (45.5 to 136.4 mcg per pound) of body weight injected slowly into a vein. The dose may be repeated after thirty minutes.

#### Missed dose—

If you miss a dose of this medicine, take it as soon as possible. However, if it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. Do not double doses.

### Storage—

To store this medicine:

- Keep out of the reach of children.
- Store away from heat and direct light.
- Do not store in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down.
- Do not keep outdated medicine or medicine no longer needed. Be sure that any discarded medicine is out of the reach of children.

## **Precautions While Using This Medicine**

It is important that your doctor check your progress at regular visits. This will allow your doctor to make sure the medicine is working properly and to change the dosage if needed.

## CARDIZEM

(Diltiazem)

If you have been using this medicine regularly for several weeks, do not suddenly stop using it. Stopping suddenly may bring on your previous problem. Check with your doctor for the best way to reduce gradually the amount you are taking before stopping completely.

Chest pain resulting from exercise or physical exertion is usually reduced or prevented by this medicine. This may tempt you to be overly active. *Make sure you discuss with your doctor a safe amount of exercise for your medical problem.* 

After taking a dose of this medicine you may get a headache that lasts for a short time. This effect is more common if you are taking felodipine, isradipine, or nifedipine. This should become less noticeable after you have taken this medicine for a while. If this effect continues or if the headaches are severe, check with your doctor.

In some patients, tenderness, swelling, or bleeding of the gums may appear soon after treatment with this medicine is started. Brushing and flossing your teeth carefully and regularly and massaging your gums may help prevent this. See your dentist regularly to have your teeth cleaned. Check with your medical doctor or dentist if you have any questions about how to take care of your teeth and gums, or if you notice any tenderness, swelling, or bleeding of your gums.

For patients taking bepridil, diltiazem, or verapamil:

- Ask your doctor how to count your pulse rate. Then, while you are taking this medicine, check your pulse regularly. If it is much slower than your usual rate, or less than 50 beats per minute, check with your doctor. A pulse rate that is too slow may cause circulation problems. For patients taking flunarizine:
- This medicine may cause some people to become drowsy or less alert than they are normally. This is more likely to happen when you begin to take it or when you increase the amount of medicine you are taking. Make sure you know how you react to this medicine before you drive, use machines, or do anything else that could be dangerous if you are not alert.

For patients taking this medicine for high blood pressure:

• Do not take other medicines unless they have been discussed with your doctor. This especially includes over-the-counter (nonprescription) medicines for appetite control, asthma, colds, cough, hay fever, or sinus problems, since they may tend to increase your blood pressure.

### **Side Effects of This Medicine**

Side Effects of This Medicine

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Not all of the side effects listed below have been reported for each of these medicines, but they have been reported for at least one of them. Since many of the effects of calcium channel blocking agents are similar, some of these side effects may occur with any of these medicines. However, they may be more common with some of these medicines than with others.

Check with your doctor as soon as possible if any of the following side effects occur:

- Less common
- o Breathing difficulty, coughing, or wheezing; irregular or fast, pounding heartbeat; skin rash; slow heartbeat (less than 50 beats per minute—bepridil, diltiazem, and verapamil only); swelling of ankles, feet, or lower legs (more common with amlodipine, felodipine and nifedipine)
- For flunarizine only--less common
- o Loss of balance control; mask-like face; mental depression; shuffling walk; stiffness of arms or legs; trembling and shaking of hands and fingers; trouble in speaking or swallowing
- Rare
- o Bleeding, tender, or swollen gums; chest pain (may appear about 30 minutes after medicine is taken); fainting; painful, swollen joints (for nifedipine only); trouble in seeing (for nifedipine only)
- For flunarizine and verapamil only--rare
- Unusual secretion of milk

## CARDIZEM

(Diltiazem)

Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. However, check with your doctor if any of the following side effects continue or are bothersome:

- More common
- Drowsiness (for flunarizine only); increased appetite and/or weight gain (for flunarizine only)
- Less common
- o Constipation; diarrhea; dizziness or lightheadedness (more common with bepridil and nifedipine); dryness of mouth (for amlodipine and flunarizine only); flushing and feeling of warmth (more common with nicardipine and nifedipine); headache (more common with amlodipine, felodipine, isradipine, and nifedipine); nausea (more common with bepridil and nifedipine); unusual tiredness or weakness

Other side effects not listed above may also occur in some patients. If you notice any other effects, check with your doctor.

## **Additional Information**

Once a medicine has been approved for marketing for a certain use, experience may show that it is also useful for other medical problems. Although these uses are not included in product labeling, calcium channel blocking agents are used in certain patients with the following medical conditions:

- Hypertrophic cardiomyopathy (a heart condition) (verapamil)
- Raynaud's phenomenon (circulation problems) (nicardipine and nifedipine)

Other than the above information, there is no additional information relating to proper use, precautions, or side effects for these uses.

#### **Brand Names**

Some commonly used brand names are:

## In the U.S.—

|   | A 1 1 47            |
|---|---------------------|
| • | Adalat <del>′</del> |

Adalat CC<sup>7</sup>

• Calan<sup>9</sup>

Calan SR<sup>9</sup>

Cardene<sup>6</sup>

Cardizem<sup>2</sup>

Cardizem CD<sup>2</sup>

Cardizem LA<sup>2</sup>

Cardizem SR<sup>2</sup>

Dilacor-XR<sup>2</sup>

DvnaCirc<sup>5</sup>

# Isoptin<sup>9</sup>

Isoptin SR<sup>9</sup>

• Nimotop<sup>8</sup>

Norvasc<sup>10</sup>

Plendil<sup>3</sup>

Procardia<sup>7</sup>

Procardia XL<sup>7</sup>

Vascor<sup>1</sup>

Verelan<sup>9</sup>

Verelan PM<sup>9</sup>

# In Canada—

- Adalat<sup>7</sup>
- Adalat PA<sup>7</sup>
- Adalat XL<sup>7</sup>
- Apo-Diltiaz<sup>2</sup>
- Apo-Nifed<sup>Z</sup>
- Apo-Verap<sup>9</sup>
   Cardizem<sup>2</sup>
- Cardizem SR<sup>2</sup>
- Isoptin<sup>9</sup>
- Isoptin SR<sup>9</sup>
- Nimotop<sup>8</sup>

- Norvasc<sup>10</sup>
- Novo-Diltazem<sup>2</sup>
- Novo-Nifedin<sup>7</sup>
- Novo-Veramil<sup>9</sup>
- Nu-Diltiaz<sup>2</sup>
- Nu-Nifed<sup>7</sup>
   Nu-Verap<sup>9</sup>
- Plendil<sup>3</sup>
- Renedil<sup>3</sup>
- Sibelium<sup>4</sup>
- Verelan<sup>9</sup>

## **CARDIZEM**

(Diltiazem)

Note:

For quick reference, the following calcium channel blocking agents are numbered to match the corresponding brand names.

This information applies to the following medicines:

- 1. Bepridil (BE-pri-dil)†
- 2. Diltiazem (dil-TYE-a-zem)±
- 3. Felodipine (fe-LOE-di-peen)
- 4. Flunarizine (floo-NAR-i-zeen)\*
- 5. Isradipine (is-RA-di-peen)†
- ‡ Generic name product may be available in the U.S.
- § Generic name product may be available in Canada
- \* Not commercially available in the U.S.
- † Not commercially available in Canada

- 6. Nicardipine (nye-KAR-de-peen) ‡†
- 7. Nifedipine (nye-FED-i-peen)‡
- 8. Nimodipine (nye-MOE-di-peen)
- 9. Verapamil (ver-AP-a-mil)‡
- 10. Amlodipine (am-LOE-di-peen)±

## Category

- Antianginal --Amlodipine ; Bepridil; Diltiazem; Felodipine; Isradipine; Nicardipine ; Nifedipine; Verapamil
- Antiarrhythmic --Diltiazem; Verapamil
- Antihypertensive --Amlodipine; Diltiazem; Felodipine; Isradipine; Nicardipine; Nifedipine; Verapamil
- Hypertrophic cardiomyopathy therapy adjunct --Verapamil
- Subarachnoid hemorrhage therapy -- Flunarizine; Nicardipine; Nimodipine
- Vascular headache prophylactic --Flunarizine; Verapamil

## **END OF INFORMATION - NOTHING FOLLOWS**